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EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,706	CHEN ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/2/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority und r 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *602* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed august 29, 2003. Currently, claims 1-20 are pending. Claims 10-18 have been withdrawn as drawn to non-elected subject matter. Claims 1-9, 19-20 have been examined on the merits.

Election/Restrictions

2. Applicant's election without traverse of Group I, Claims 1-9, 19-20 in the Paper filed August 29, 2003 is acknowledged.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims

and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Priority

3. This application claims priority as a 371 of PCT/CA00/00716, filed June 14, 2000. PCT/CA00/00716 is a non-provisional of 60/139,260 June 15, 1999.

It is noted that the provisional application fails to disclose probes of SEQ ID NO: 5, 6. Thus, Claims 6-9 which require the particular probes of SEQ ID NO: 5 and 6 are entitled to the priority date of June 14, 2000.

Drawings

4. The drawings are acceptable.

Claim Objections

5. Claims 7, 9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

For example, Claim 6 is directed to a probe comprising nucleotides 597-677 of SEQ ID NO: 1. SEQ ID NO: 5 is the same sequences as nucleotides 597-677 of SEQ ID NO: 1. The claims are both drawn to open, having and comprising claim language. Both sequences are 81 nucleotides in length, thus, the claims appear to be identical scope. Similarly, Claim 9 does not further limit Claim 8.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-9, 19-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acid molecules comprising SE QID NO: 1 or a diagnostic fragment thereof. The claims are also drawn to complimentary sequences to SEQ ID NO:1, sequences which can hybridized, sequences which have substantial sequence homology and nucleic acid sequences which is an analog.

The specification teaches a novel marker specific for *E. coli* serotypes O157:H7, O157:NM and O55:H7. The specification teaches the marker of 1583 nucleotides (SEQ ID NO: 1).

The specification teaches that the term "diagnostic fragment" is any fragment of SEQ ID NO: 1 that is useful in a diagnostic assay to detect *E. coli* serotypes O157:H7, O157:NM and O55:H7 (page 3).

The specification teaches that "a nucleic acid sequence which has substantial sequence homology" means a nucleic acid sequence which has slight or inconsequential sequence variations from SEQ ID NO: 1 (page 3)

The specification also teaches that natural variations may exist in the sequence of certain isolates which may be attributable to local mutations or structural modifications (page 4).

The specification teaches that an analog may have improved properties over SEQ ID NO: 1.

The art teaches a sequence which comprises a nucleic acid 99.9% similar with SEQ ID NO: 1 in a larger sequence (Genbank Accession Number AE005661, March 2001). SEQ ID NO: 1 aligns with the complement of positions 12782-14365. The description indicates that this region is within a gene Z5901 which is a putative enzyme. The gene product is a much larger region than SEQ ID NO: 1. The gene region is 7938-14279.

The art teaches a sequence which comprises a nucleic acid 99.9% similar with SEQ ID NO: 1 in a larger sequence (Genbank Accession Number AP002569, March 2001). SEQ ID NO: 1 aligns with the complement of positions 56734-58317.

The language of the claim indicates that the claim is drawn to a genus, i.e., any nucleic acid which minimally contains SEQ ID NO: 1 within it including any full length gene which contains the sequence.

A search indicates that SEQ ID NO: 1 is a novel and unobvious sequence. There is a single species explicitly disclosed (a molecule consisting of SEQ ID NO: 1 that is within the scope of the claimed genus).

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from

its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, Applicant has defined only a fragment of a nucleic acid sequence which has been deemed to be a marker for *E. coli* . serotypes O157:H7, O157:NM and O55:H7 (page 3).

The present claim encompasses full-length genes and cDNAs that are not further described. There is substantial variability among the species of DNAs encompassed within the scope of the claims because SEQ ID NO: 1 is only a fragment of any full-length gene or cDNA species. Here the specification discloses only a single common structural feature shared by members of the claimed genus, i.e., SEQ ID NO: 1. Since the claimed genus encompasses genes yet to be discovered, natural variants and sequence which have "substantial sequence homology", the disclosed structural feature

does not "constitute a substantial portion" of the claimed genus. As seen in the post filing date art, SEQ ID NO: 1 is embedded within a gene designated Z5901which is a putative enzyme. The instant specification fails to disclose the full gene or coding sequence of Z5901. Thus, the instant claim reads on a gene, namely Z5901 which was not disclosed by the instant application. Therefore, the disclosure of SEQ ID NO: 1 does not provide an adequate description of the claimed genus. Similarly, the claims are directed to diagnostic fragments which are partial fragments of SEQ ID NO: 1 which may be embedded within larger fragments which are not described.

Weighing all factors, 1) partial structure of the DNAs that comprise SEQ ID NO; 1, 2) the breadth of the claim as reading on genes yet to be discovered, 3) the lack of correlation between the structure and the function of the genes; in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the genus of DNAs which comprise SEQ ID NO: 1.

With specific respect to the hybridization embodiments, "a nucleic acid that can hybridize to the sequence show in SEQ ID NO: 1" and "a nucleic acid sequence which is complementary to the sequence show in SEQ ID NO: 1," the claims fail to meet the written description requirements. As provided in Example 9 of the Written Description Guidelines, a claim to a nucleic acid which hybridizes to SEQ ID NO: 1, fails to meet the requirements for written description. A person of skill in the art would expect substantial variation among species encompassed within the scope of the claims because the claims fail to set forth any hybridization conditions or a function of the DNA. Thus, a

representative number of species have not been disclosed. The claim does not specify any stringency conditions. The claims are broad and read on virtually any nucleic acid since the genus is expect to yield structurally unrelated nucleic acid molecules.

With respect to sequences which have substantial sequence homology, the genus of nucleic acids encompassed by the claims includes natural variations which may exist in the sequence of certain isolates which may be attributable to local mutations or structural modifications (page 4). The specification discloses only one species within the scope of the genus, namely SEQ ID NO: 1. There is no description of the mutational sites that exist in nature, and there is no description of how the structure of SEQ ID NO: 1 relates to the structure of any strictly neutral alleles. The general knowledge in the art concerning isolates, variations does not provide any indication of how the structure of one isolate or variation is representative of unknown alleles. The nature of alleles, variations, analogs, and isolates is that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others. The common attributes of the genus are not provided. Once of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of the genus is not representative of the variants of the genus and is insufficient to support the claim.

It is noted that claims drawn to nucleic acids consisting of SEQ ID NO: 1, 3, 4, 5, 6 would overcome the written description rejection because they would be limited to the particular sequence and would not encompass any larger sequences.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-3, 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Boehringer Mannheim (1997 Biochemicals Catalog, page 122).

Boehringer Mannheim teaches a hexanucleotide mixture, a primer for cDNA synthesis which comprises polyT10 or polyT15. The hexanucleotide mixture would comprise nucleic acid molecules which were diagnostic fragments of SEQ ID NO: 1. The term "diagnostic fragment" is any fragment of SEQ ID NO: 1 that is useful in a diagnostic assay to detect *E. coli* serotypes O157:H7, O157:NM and O55:H7 (page 3 of specification). The specification also teaches that primers contain from about 5-50 nucleotides in length. The hexanucleotide mixture would thus be able to amplify SEQ ID NO: 1, as it is a portion of SEQ ID NO: 1 (limitations of Claim 1, 2, 3, 5). Moreover, the primer dT10 would hybridize to the sequence of SEQ ID NO: 1 at position 8-15 which is 8 T nucleotides (limitations of Claim 2). Thus, Boehringer Mannheim teaches every limitation of the claimed invention.

8. Claims 1-3, 5, 19-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796, December 12, 1995).

The term "diagnostic fragment" is any fragment of SEQ ID NO: 1 that is useful in a diagnostic assay to detect *E. coli* serotypes O157:H7, O157:NM and O55:H7 (page 3 of specification). The specification also teaches that primers contain from about 5-50 nucleotides in length.

Brennan teaches oligonucleotides having 10 nucleotides each (10-mers)(limitations of Claim 1-3, 5). The oligonucleotides represent every possible permutation of the 10-mer oligonucleotide. Brennan teaches the 10-mers are placed on an array (col. 9, lines 48-60)(limitations of Claims 19-20). Therefore, Brennan teaches diagnostic fragments of SEQ ID NO: 1, complimentary nucleic acid sequences and portion of SEQ ID NO: 1 which are 10 nucleotides in length.

9. Claims 1-3, 5 are rejected under 35 U.S.C. 102(a) as being anticipated by Mahairas et al (Genbank AQ231499, September 1998).

Mahairas et al. (herein referred to as Mahairas) teaches a nucleic acid in a vector which comprises the 21 nucleotides of SEQ ID NO: 1. Nucleotides 1120-1140 of SEQ ID NO: 1 are 100% identical to nucleotides 447-427 of Mahairas. It is noted that the instant specification teaches that diagnostic fragments encompass SEQ ID NO: 3 and 4, which are overlapping with the instant region. Thus, nucleotides 1120-1140 is a diagnostic fragment of SEQ ID NO: 1. The nucleic acid of Mahairas comprises this

diagnostic fragment of SEQ ID NO: 1 (limitations of Claim 1-3, 5). Thus, since Mahairas teaches every limitation of the claims, Mahairas anticipates the claimed invention.

10. Claims 6-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Blattner et al. (US Pat. 6,365,723, April 2002).

As noted above, provisional application 60/139,260 does not disclose SEQ ID NO: 5 or 6 as probes for E. coli. Thus, Claims 6-9 are entitled to the benefit of priority date of June 14, 2000.

Blattner teaches a nucleic acid sequence of SEQ ID NO: 242 which is 92.4% identical to SEQ ID NO: 1. Nucleic acid sequence 242 of Blattner is 100% identical over the 81 nucleotides of SEQ ID NO: 5. Nucleotides 27768-27688 are 100% identical to instant SEQ ID NO: 5. Thus, Blattner teaches a nucleic acid probe comprising SEQ ID NO: 5 (limitations of Claims 6 and 7). Moreover, Blattner teaches Nucleic acid sequence 242 of Blattner is 100% identical over the 96 nucleotides of SEQ ID NO: 6. Nucleotides 27304-27209 are 100% identical to instant SEQ ID NO: 6. Thus, Blattner teaches a nucleic acid probe comprising SEQ ID NO: 6 (limitations of Claims 8 and 9).

Allowable Subject Matter

11. Claims drawn to a nucleic acid consisting of SEQ ID NO: 1 would be novel and unobvious. The instant specification demonstrates that SEQ ID NO: 1 is a marker for *E. coli* serotypes O157:H7, O157:NM and O55:H7. As seen in Figure 3, a gel electrophoresis of PCR products amplified using PCR assay illustrates the specific

detection of for *E. coli* serotypes O157:H7, O157:NM and O55:H7. Moreover, nucleic acids consisting of SEQ ID NO: 3, 4, 5, 6 would be allowable for amplification and probing of SEQ ID NO: 1. The speciation teaches that using the primers of Table 3, the inventors have demonstrated that these primers are specific for the *E. coli* serotypes O157:H7, O157:NM and O55:H7 but are not specific for 199 other E. coli strains belonging to 60 serotypes and 59 isolates belonging to 44 non- E. coli species (Example 1)(Page 10).

Conclusion

12. No claims allowable.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Goldberg
Patent Examiner
November 17, 2003